



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Request for Letters of Interest (LOI) for NCI-MATCH Laboratories

**SUMMARY:** The National Cancer Institute (NCI) in collaboration with the NCI Molecular Analysis for Therapy Choice (MATCH) trial leadership (NCT 02465060) invites applications for Clinical Laboratory Improvements Program (CLIA) certified/accredited laboratories that test tumor specimens from patients utilizing Next Generation Sequencing (NGS) assays to participate in the NCI MATCH trial. The NCI MATCH trial has implemented a new process for identifying patients for arms with rare variant eligibility criteria. Laboratories will contact any of the approximately 1100 sites that have activated NCI MATCH if a specimen sent from one of these sites has a rare variant that would potentially make the patient eligible for one of the treatment arms open in this initiative.

**DATES:** LOIs should be submitted to the National Cancer Institute (NCI), National Institutes of Health (NIH) on or before 5:00 P.M. EST on January 31, 2018.

**ADDRESSES:** Submit LOIs by e-mail to [NCIMATCHLabApps@nih.gov](mailto:NCIMATCHLabApps@nih.gov) .

9609 Medical Center Drive, 3 West, Room 526, MSC 9728, Rockville, MD 20892.

**FOR FURTHER INFORMATION:** Questions about this request for LOIs should be directed to **NCIMATCHLabApps@nih.gov**. James V. Tricoli **tricolij@mail.nih.gov** can also provide further information.

**SUPPLEMENTAL INFORMATION:**

NCI-MATCH aims to establish whether patients with tumor mutations, amplifications or translocations in one of the genetic pathways of interest are likely to derive clinical benefit (primary objective: objective response; secondary objective: progression-free survival of at least 6 months) if treated with agents targeting that specific pathway in a single-arm design (see current arms below).

Patients with histologically documented solid tumors, lymphomas and multiple myeloma whose disease has progressed following at least one line of standard systemic therapy or for whom no standard therapy exists are eligible if they meet the eligibility criteria for the trial. Further information about the NCI-MATCH trial may be found at <http://ecog-acrin.org/trials/nci-match-eay131>.

The selected collaborating laboratories may only act (i.e. refer patients) on any of the rare variant arms for which their assay reports actionable mutations of interest (aMOIs). The assay must also report all exclusionary variants for the arm unless these occur at a frequency of < 1% in cancer patients.

CLIA accredited/certified laboratories located in the United States may be considered for addition to the laboratory network.

## Letter of interest (LOI) and Collaboration Agreement

Candidate laboratories should submit a letter of interest to

**NCIMATCHLabApps@nih.gov**, stating:

- Statement of interest in the proposed activity
- Laboratory name
- Lead contact name, address, email address, and telephone number
- CLIA certification number
- Assay name
- Brief description of assay
  - Sensitivity and specificity for SNVs, indels, CNV, fusions
  - Method of analysis
  - Platform and variant calling
- Number of assays per month
- Number of patients whose assay results would make them potentially eligible for the rare variant arms (below) in the last 6 months
- Willingness to contact sites regarding results with a rare variant potentially eligible for NCI MATCH
- Willingness to sign a collaboration agreement with NCI and to share data and publication rights
- Which arms the laboratory is prepared to address.

The arms that are included in the rare variant protocol amendment are:

<b>Rare Variant Candidate</b>	<b>MATCH SubProtocol (Agent)</b>
AKT1 mut	EAY131-Y (AZD5363)
NF2 loss	EAY131-U (Defactinib)
MET amplification	EAY131-C1 (Crizotinib)
BRAF V600	EAY131-H (Dabrafenib + Trametinib)
SMO/PTCH1	EAY131-T (Vismodegib)
BRAF non V600	EAY131-R (Trametinib)
EGFR T790M	EAY131-E (AZD9291)
ALK translocation	EAY131-F (Crizotinib)
cKIT mutation	EAY131-V (Sunitinib)
EGFR mutation	EAY131-A (Afatinib)
ROS1 translocation	EAY131-G (Crizotinib)
GNAQ/GNA11	EAY131-S2 (Trametinib)
MET exon 14 skipping	EAY131-C2 (Crizotinib)
NTRK fusions	EAY131 Z1E (Loxo101)

MTOR mutations	EAY131-L (MLN0128)
TSC1 or TSC2 mutations	EAY131-M (MLN0128)
CCND 1,2,3 amplifications	EAY131-Z1B (Palbociclib)
CDK4 or CDK6 amplification	EAY131-Z1C (Palbociclib)
DDR2 mutation	EAY131-X (Dasatinib)

Following an acceptable eligibility review to the NCI MATCH screening committee, the laboratory would execute a confidentiality agreement with the NCI and will be provided with a detailed list of eligibility and exclusion variants for arms in which the lab has interest. The lab would then be required to submit an application within 3 months for review by the NCI-MATCH steering committee. Candidate laboratories will be required to meet the following general requirements:

- Testing must be performed in a CLIA-certified or -accredited laboratory located in the United States.
- Assays must be on tumor tissue only (including lymphoma and myeloma). Assays using circulating nucleic acids will not be accepted at this time.
- Laboratory NGS panels must be analytically and clinically validated, with performance characteristics as follows:
  - Specificity at least 99% for single nucleotide variants, indels
  - Sensitivity at least 95% for single nucleotide variants, indels

- Sensitivity of 90% for copy number variants (state fold of copy number variants that can be detected with 90% sensitivity)
- 99% reproducibility between sequencers (if more than one sequencer is used) and between operators
- Lower limit of detection for SNV, indels, CNV must be stated.

Laboratories must supply the following information in their application:

- Lower limit of % tumor accepted, and whether (and which) enrichment procedures are employed
  - Whether the lab archives images of slides from the tumor
  - Whether the lab also runs germline as well as tumor with the assay (a simultaneous germline sequencing is not required by NCI MATCH)
  - A detailed description of assay procedures, including starting material, extraction of nucleic acids, quality assurance, quality metrics, data analysis and filters must be supplied.
- Laboratory NGS test panels must interrogate actionable mutations of interest (aMOIs) required for enrollment into the Rare Variant Arms (see table above). Applicant laboratories must state the MATCH arms in which they would like to participate.
  - Academic laboratories must be located at a center that participates in NCI MATCH.
  - As it is important that the dataset used for analysis in NCI MATCH be as robust as possible, the laboratory NGS test will require qualification, during which the

performance of the laboratory will be compared with the NCI-MATCH central laboratory test to ensure good agreement with that assay. Concordance between the results from each lab and results of the NCI MATCH NGS assay run on an archived specimen will be tracked; if concordance falls below 90% for SNVs and indels, or 80% for CNVs, the laboratory must be willing to address these issues with the NCI MATCH team. If they cannot be addressed to the satisfaction of the NCI MATCH team, the laboratory may be eliminated from participation in NCI MATCH.

- Laboratories shall NOT advertise that they are screening laboratories for MATCH eligibility. Any press release or public disclosure requires clearance by NCI and NCI MATCH.
- Laboratories must agree to use the existing workflow established by the NCI MATCH trial to identify patients for the Rare Variant Arms. This includes use of the MATCH Rare Variant template to identify aMOIs for submission to MATCHbox.
  - Laboratory results of NGS assays done for clinical care will be the subject of this initiative. There is no funding for “screening” a patient for MATCH.
  - Laboratories must notify NCI MATCH sites that the laboratory results would potentially allow the patient to be eligible for NCI MATCH.
  - Laboratories must track how many assays per week detect rare variants that could make a patient eligible for NCI MATCH.

- If the clinician presents the MATCH study and the patient is eligible and desires to enter the study, the laboratory must agree to fill out a spreadsheet that can be used to put the results into the informatics system that assigns treatment in NCI MATCH (MATCHbox).
- Laboratories must have a way to answer questions from NCI MATCH sites about their assay and must have a contact person for optimal communication with the NCI MATCH team.
- Prior to participation, laboratories must enter into a collaboration agreement with NCI. A sample agreement is available upon request. As part of such a collaboration agreement, laboratories must agree to provide the licensing rights described in the CTEP IP Option to the Pharmaceutical Collaborators who provided agents for the NCI MATCH trial ([https://ctep.cancer.gov/branches/rab/intellectual\\_property\\_option\\_to\\_collaborators.htm](https://ctep.cancer.gov/branches/rab/intellectual_property_option_to_collaborators.htm)), as well as agree to the data sharing and publication rights consistent with those agreements.
- No reimbursement for these activities (testing or notification of sites of NCI MATCH eligibility) exists.

Qualified laboratories serving underserved populations are encouraged to participate.

How to apply:

1. Submit letter of interest (LOI) as described above under “Letter of Interest and Collaboration Agreement” to **NCIMATCHLabApps@nih.gov**



2. LOIs will be accepted until January 31, 2018 at 5:00PM Eastern Time. LOIs will be reviewed on a monthly basis, with those arriving by the 15<sup>th</sup> day of the month being reviewed and answered by the 15<sup>th</sup> day of the following month.
3. Notification of acceptance, non-acceptance or questions from Steering Committee will be sent to the designated contact person as soon as the LOI has been reviewed. This notification will include further instructions if a full application is invited.
4. Applications that have not been submitted within 3 months of notification of acceptance will be de-activated, and a new LOI must then be submitted if the laboratory wishes to participate in NCI MATCH.
5. DO NOT send a full application until you are invited to do so.

Review criteria for LOI:

- Laboratory is a CLIA certified or accredited laboratory within the United States.
- Academic laboratories must have NCI MATCH open at their site.
- Laboratory has adequate sensitivity, specificity.
- Laboratory tests tumor tissue for rare variants as described in NCI MATCH.
- Laboratory agrees to provide needed information for evaluation of the analytical validity of the test.
- Laboratory is likely to refer at least 100 patients to NCI MATCH based on detection of rare variants in the past.
- Laboratory agrees to contact sites regarding NCI MATCH eligibility.
- Laboratory agrees to a collaboration with NCI as detailed above.

Review criteria for full application:

- Laboratory NGS assay interrogates inclusionary and all exclusionary variants for arms in which the laboratory will participate.
- Laboratory supplies evidence that the assay meets analytical requirements as detailed above.
- Laboratories are capable of contacting clinical sites, tracking activity, and of referring at least 100 patients to the study based on detection of rare variants in the past.
- Laboratories agree to execute a collaboration agreement with NCI, as well as to data sharing and sharing publication rights.
- Laboratories agree to abide by the procedures in place for the MATCH study and to collaborate fully with the MATCH team.

For more information, contact **NCIMATCHLabApps@nih.gov**

Dated: July 20, 2017

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